REMARKS

I. BACKGROUND

On page 17 of the Specification, Applicants have deleted the phrase "through SEQ ID NO: 5521". To facilitate prosecution, Applicants have amended the pending claims to recite the term "isolated" instead of "substantially purified". Support for the amendment can be found, for example, at page 25, line 1 through line 19, page 66, line 25 through page 67, line 6 and page 67, line 25 through page 68, line 7. Claims 1 through 3 have been amended to recite the phrase "or its complement". Support for the amendment can be found, for example, at page 10, lines 1-2, page 18, page 18, lines 14-18, and page 20, line 15. Claim 4 has been canceled, without prejudice, to facilitate the present prosecution.

The claims of the present application recite the sequence of an Expressed Sequence Tag ("EST") and its complement. That EST was derived from a cDNA library of soybean DNA (specifically from soybean seeds and pods) (Specification at 24). Facts pertinent to this EST, and ESTs as a class of substances that also relate to issues involved in this case, are set forth here.

DNA contains the information required by cells to synthesize all of the proteins they use. In eukaryotic organisms, such as soybeans, a very small percentage of genomic DNA is actually used to code for protein products needed by the cell or organism. In humans, for instance, coding DNA is believed to account for about three percent (3%) of the total human genome.

In the first step of cellular protein synthesis, a strand of mRNA is synthesized using genomic DNA as a template. The mRNA is initially closely related to the strand of DNA which served as the template for its synthesis; there is a one-to-one correspondence between the bases in the DNA and the mRNA. In eukaryotic organisms some of the bases in the mRNA, however, are subsequently removed by other components of the cell. These excised bases correspond to noncoding bases in the template DNA and are called introns. The information contained in the introns is not used in protein synthesis. The bases remaining in the edited mRNA serves as a template for protein synthesis and correspond to the coding regions of the genomic DNA.

A process known as *reverse transcription* can be used to create a strand of DNA that mirrors the edited strand of mRNA. The strand of DNA resulting from this reverse transcription is called cDNA (complementary DNA). It is identical to the original strand of DNA, except that it contains no introns.

The EST recited in the present claims corresponds to a part of a soybean genome, which is transcribed *in vivo* (mRNA) and translated to express a protein.[1] While all of the information concerning the full length gene associated with the recited EST and the related expressed protein are not yet known, the nucleic acid sequence identified as SEQ ID No. 1 inherently has a real biological function in soybean because it corresponds to a mRNA sequence that is translated into a protein sequence.

The EST identified as SEQ ID No. 1 was isolated from a cDNA library prepared from young seeds that are collected from young pods (5 to 15 days after flowering). Joseph R. Byrum and Gregory R. Heck selected the tissue (*i.e.*, young seeds that are collected from young pods). Thomas J. La Rosa prepared the cDNA library. These individuals were considered inventors based on those contributions.

II. THE APPLICATION MEETS THE UTILITY REQUIREMENT OF 35 U.S.C. § 101

Pending claims 1-4 were rejected under 35 U.S.C. § 101 because the claimed invention was allegedly not supported by either a "specific asserted utility" or a "well-established utility". The Examiner stated:

> there is no apparent, *immediate* benefit to the public. The only readily apparent *immediate* utility for the disclosed EST is characterization of the EST itself in terms of map location, identity of corresponding sequence polymorphisms, sequence of corresponding mRNA and polypeptide, *etc.* This sole immediate utility constitutes research on the claimed product itself, which is a non-statutory utility, in order to determine a specific statutory utility for the claimed invention.

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[1] EST sequences typically represent automated single run sequence. Such automated single run sequence often have a 2-3% error or ambiguity rate.

Office Action at 4, *citing Brenner v. Manson*, 383 U.S. 519, 535, 148 U.S.P.Q. 689, 696 (1966). This analysis misstates the nature of the asserted uses, ignores other disclosed utilities and misapplies the doctrine of "practical utility" developed by the courts after *Brenner v. Manson*.

A. ESTs inherently have utility that satisfies 35 U.S.C. §101.

ESTs are fundamentally different from non-biological chemicals that have been the subject of prior decisions under 35 U.S.C. § 101. Chemicals involved in prior "utility" adjudications have not possessed any known function in nature or industry. All ESTs are known to correspond to part of a mRNA molecule that performs some function in nature; they produce peptides used by the cell or organism. This is not merely an academic difference; it has resulted in the growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs.[2]

These expenditures for ESTs are driven largely by the fact that they are known to serve a function in nature. The utility requirement of Section 101 is merely a shorthand of attributing "real-world" value to claimed subject matter. *Nelson v. Bowler & Crossley,* 626 F.2d 853, 856, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980). To contend that ESTs lack "real world" value that establishes "utility" in its patent law sense, requires ignoring industries that the patent system was created to serve and to foster.

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[2] Many biotechnology companies derive significant revenue from EST databases. Celera Genomics has licensed its "Human Gene Index" EST database to Amgen, Inc., Novartis, and Pharmacia & Upjohn. Incyte Pharmaceuticals reported 1998 revenues from subscriptions to its EST databases, at $105.6 million. Gene Logic, Inc. licenses its EST databases to numerous companies such as Procter & Gamble Pharmaceuticals and Organon, N.V. and has entered an agreement with Affymetrix, Inc. in early 1999 to build a large commercial EST database for drug development. Exelixis Pharmaceuticals Inc. and Bayer AG entered a genetic collaboration agreement in 1998 that gives Bayer a license to Exelixis' "FlyTag" Drosophila EST database and obligates Exelixis to develop new pest species EST databases for Bayer. DuPont signed a five-year deal with Lynx Therapeutics to use Lynx's technology to organize DuPont's extensive crop EST databases and provide genomic maps for crops. Human Genome Sciences also licenses its proprietary EST databases to companies and public scientific institutions. Articles reporting the foregoing information on commerce in ESTs are listed in the accompanying Information Disclosure Form.

B. The present application discloses unchallenged specific uses of the claimed invention in its current form.

Even if the well-known fact of biological function is deemed insufficient for purposes of statutory utility, the asserted utilities in the specification are themselves sufficient. Utility under 35 U.S.C. §101 is a question of fact. *Newman v. Quigg*, 877 F.2d 1575, 1581, 11 U.S.P.Q.2d 1340, 1345 (Fed. Cir. 1989). Statutory "utility" for an invention is present "where specific benefit exists in [the claimed invention's] currently available form . . .". Utility can not reside in a compound's potential role as an of object use-testing. *See In re Ziegler*, 992 F.2d 1197, 1203, 26 U.S.P.Q.2d 1600, 1605 (Fed. Cir. 1993); *In re Kirk*, 376 F.2d 936, 945, 153 U.S.P.Q. 48, 56 (C.C.P.A. 1966).

In the context of a reduction to practice (the subject patent application), "practical utility for the invention is determined by reference to, and a factual analysis of, the disclosure of the application". *In re Ziegler*, 992 F.2d at 1201, 26 U.S.P.Q. 2d at 1603 (quoting *Cross v. Iizuka*, 753 F.2d 1040, 1044, 224 U.S.P.Q. 739, 742 (Fed. Cir. 1985)). Utilities asserted in the specification must be accepted as factually sound unless the Patent Office cites information that undermines the credibility of the assertion. *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). Here, a number of utilities have been asserted that are not solely "use based" and that the Patent Office has not challenged. Those assertions of utility are alone sufficient to satisfy 35 U.S.C. §101.

1. The Asserted Utilities.

Five utilities asserted in the specification and listed by the Examiner were: (1) use as a probe for identifying polymorphism (Specification at, for example page 28, line 3 through page 36, line 10); (2) use as a probe for detecting a physical map location (Specification at, for example, page 38, line 10 through line 22); (3) use as a probe or source of PCR primers to isolate other nucleic acids (Specification at, for example, page 24, line 13 through page 27, line 8); (4) use as an antisense inhibitor (Specification at, for example, page 64, line 23 through page 65, line 25); and (5) use as a probe to isolate proteins that might bind to the EST sequence (Specification

at, for example, page 43 line 4 through page 44, line 21). The Examiner contends that all of the foregoing utilities are non-specific and require additional research on the molecule itself to establish utility. He states, without any factual support, that the only readily apparent immediate utilities "constitutes research on the claimed product itself, which is non-statutory utility". *See In re Kirk*, 376 F.2d 936, 945, 153 U.S.P.Q. 48, 56 (C.C.P.A. 1966); *Brenner v. Manson*, 383 U.S. at 535, 148 U.S.P.Q. at 696. As a result the Patent Office concludes, "there is no apparent *immediate* benefit to the public".[3] That contention and that conclusion are factually unsupported and are wrong.

2. The Disclosed Utilities are Specific to the Recited EST Sequence.

The Examiner has contended that additional knowledge is necessary before the sequence can "be used for a specific purpose". Certainly, additional knowledge about the nucleic acid sequence and the protein product coded by it, in whole or in part, may be needed before the biological function of the recited sequence in the cell can be fully defined. Those unknown functions, however, are not the asserted utilities in this case. The utilities asserted here arise because of the simple fact that the recited sequence corresponds to a mRNA molecule that has some function in the cell because it is a coding sequence. That knowledge alone makes the recited sequence immediately useful as a tool in commercial and experimental activities. Moreover, evidence demonstrating utility for any purpose is enough to show reduction to practice. *See Shurie v. Richmond*, 699 F.2d 1156, 1159, 216 U.S.P.Q. 1042, 1045 (Fed. Cir. 1983). Indeed, a party need not demonstrate commercial acceptability, but only that the product produced by the process can be employed in some useful fashion. *See Shurie v. Richmond,* 699 F.2d at 1160, 216 U.S.P.Q. at 1045.

The first utility is the use of the claimed molecules as probes for identifying the presence or absence of polymorphisms. (Specification at page 28, line 3 through page 35, line 3); "In one

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[3] It is unclear to the Applicant who the Examiner is envisioning as not receiving immediate benefit.

sub-aspect, such an analysis is conducted by determining the presence and/or identity of polymorphism(s) by one or more of the nucleic acid molecules of the present invention..." (Specification at page 28, lines 3-5); "Polymorphisms are useful, through linkage analysis, to define genetic or physical distances between polymorphic traits. A physical map or ordered array of genomic DNA fragments in a desired region containing the gene may be used to characterize and isolate genes corresponding to desirable traits." (Specification at page 35, lines 4 through 7). This utility as a "tool" is not the same as employing the recited sequence as an object of use-based experimentation. It is instead a use of the claimed substance to screen populations of plants to determine the presence or absence of a polymorphism. That use develops information about the plant as stated in the specification not additional information about the claimed sequence. No additional knowledge about the recited sequence or its biological functions is necessary to warrant, prompt, or enable use of the recited molecules in this manner.

The Examiner states that the Applicant has not established that there are polymorphisms linked to the corresponding genomic location. That is irrelevant. The issue is whether the claimed molecules could be used to identify polymorphisms -- *i.e.* screen for the presence or absence of polymorphism. Absent some evidence that the claimed invention could not be used to detect the presence or absence of a polymorphism, this assertion of utility satisfies the requirements of 35 U.S.C. §101. *See In re Brana*, 51 F.3d at 1566, 34 U.S.P.Q.2d at 1441. The Examiner's attention is particularly drawn to the references cited within the Specification at page 35, line 26 through page 36, line 10. Applicants submit that a *prima facie* utility rejection has not been made.

Screening for polymorphisms is useful in plant breeding. For example, the EST can be used as a primer or to generate primers used to screen subsequent generations of soybean progeny from a breeding program using, as a parent, the soybean line used to generate the cDNA from which the EST was identified. No further additional knowledge is required to start this use. That is not to say, of course, that additional information will not be obtained and, perhaps, be of value. That is simply irrelevant.

The second utility is use as a probe for detecting a physical map location.[4] (Specification at page 35, line 4 through page 36, line 10); "A physical map or ordered array of genomic fragments ... may be used to characterize and isolate genes corresponding to desirable traits." (Specification at page 35, lines 5-7); "Through genetic mapping, a fine scale linkage map ... can be screened with molecular markers for the desired trait." (Specification at page 35, lines 17 through 19). The use of the claimed molecules for mapping the location of the gene is not a characterization that "constitutes research on the product itself" it is a use of the claimed product to perform a valuable real world activity; locate the position of a gene on a physical or genetic map. That mapping is itself useful, for example, in plant breeding.

The third utility is the use of the claimed molecules as a probe for other molecules or as a source of PCR primers to isolate other nucleic acids. It is not clear to the Applicants, which, if any, of the Examiner's recited concerns (Office Action, at 4, first full paragraph) would be applicable to this use of the claimed molecules. The claimed molecules could plainly be used to isolate other molecules. For example, the specification discloses that the claimed molecules can be used to isolate nucleic acid molecules such as promoters, which are associated with the claimed nucleic acid molecules ("Promoter sequence(s) and other genetic elements ... associated with one or more of the disclosed nucleic acid sequences can also be obtained using the disclosed nucleic acid sequences provided herein." (Specification at page 25, line 20 through line 23; page 25, line 20 through page 26, line 4)). No evidence or reasoning has been provided to make a *prima facie* showing that this utility is not credible.

The fourth utility referred to by the Examiner is the use of the claimed molecules as an antisense inhibitor ("Antisense approaches are a way of preventing or reducing gene function by targeting the genetic material. ... It is understood that protein synthesis activity in a plant cell may be reduced or depressed by growing a transformed plant cell containing a nucleic acid

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[4] While the Examiner has focused on the utility of the claimed molecules to detect a "physical map location," the claimed molecules are also capable of being used to detect a "genetic map location."

molecule whose non-transcribed strand encodes a protein synthesis enzyme" (Specification at page 64, line 23 through page 65, line 25)). It is not clear to the Applicants, which, if any, of the Examiner's concerns are applicable to this utility. If the Examiner is asserting that a person skilled in the art would not find this use credible, evidence supporting that contention must be provided.

The fifth utility identified by the Examiner is the use of the claimed molecules to identify proteins that might bind to the sequence ("Interaction mating has been used to examine interactions between small sets of tens of proteins. ... It is understood that the protein-protein interactions of proteins or fragments thereof may be investigated in the two-hybrid system and that any of the nucleic acids molecules of the present invention that encode proteins or fragments thereof may be used to transform yeast in the two hybrid system." Specification at page 45, line 4 through 5 and line 17 through 21). At issue is whether the claimed molecules could be used to screen or identify proteins to which they bind. Again, if the Examiner is contending that such a utility is not credible he must provide evidence of it.

The Examiner has chosen to ignore the following asserted utilities, any one of which is sufficient to satisfy the statutory utility requirement:

- the claimed nucleic acid molecules can measure the level of an mRNA in a sample (Specification at, for example, page 27, line 9 through line 25 and page 36, line 19 through page 38, line 9);
- the claimed nucleic acid molecules can be used in connection with microarrays (Specification at, for example, page 40, line 14 through page 41, line 18);
- the claimed nucleic acid molecules may be introduced into a cell, such as plant cell (Specification at, for example, page 45, line 22 through page 65, line 25);
- that antibodies can be raised against such proteins or fragments thereof (Specification at, for example, page 20, line 19 through page 24, line 2); and

- nucleic acid sequences of molecules can be compared to the nucleic acid sequences of other molecules (Specification at, for example, page 20, line 19 through page 24, line 2).

The specification plainly states that the claimed nucleic acid molecules can measure the level of a mRNA in a sample ((Specification at page 36, line 19 through page 38, line 9); "In one aspect of the present invention, an evaluation can be conducted to determine whether a particular mRNA is present." (Specification at page 36, lines 19 through 20)). No further information about the molecule is needed for this purpose. Measuring the level of expression provides information about a plant's response to various conditions such as stress or developmental stages.

The disclosure also sets forth other uses for the claimed nucleic acid molecules. These other uses of the claimed nucleic acid molecules include: using the claimed nucleic acid molecules in conjunction with microarrays; introducing the claimed nucleic acid molecules in cells, particularly plant cells and comparing the nucleic acid sequences of the claimed nucleic acid molecules with other nucleic acid sequences. Indeed, with the latter use no additional knowledge could be necessary as this is exactly what they did when the Examiner rejected claim 4 over Shen *et al.* (Office Action at 13, last paragraph). Again, no additional knowledge about the recited sequence is needed for any of these purposes and each, by itself is sufficient to support utility.

It is unclear to the Applicant exactly what the Examiner means when he states that characterization of the EST itself includes the sequence of the corresponding mRNA and polypeptide sequence. (Office Action at 4). It is possible that the Examiner means that the EST can be used to isolate a corresponding mRNA, which can be sequenced, and from that sequence the protein sequence can be derived. If this is what the Examiner is saying, we agree. However, such a use for the claimed molecules does not "constitute[s] research on the product itself" it is a use of the claimed product to obtain other products and thus satisfies the statutory utility requirement.

The Examiner has stated that the uses described by the Applicant are non-specific in that other soybean ESTs would apply equally to any uncharacterized nucleic acid molecule from soybean. The claimed molecules, however, are not uncharacterized. Their nucleic acid sequence is disclosed. Moreover some other soybean EST would not, unless it was derived from the same gene, map to the same genomic location, measure the same mRNA population *etc.* The mere fact that two molecules might have the same use doesn't render them without utility. It would make no sense to reject a new antibiotic compound because other compounds have the same utility -- *i.e.,* the ability to inhibit bacterial growth.

3. The Utility Rejection Violates PTO Utility Guidelines

Any assertion by applicants of utility must be accepted by the PTO unless it would not be considered "credible" by a person of ordinary skill in the art. MPEP § 706.03(a)(1). If the PTO contends that the asserted utility is not credible, the examiner must present a *prima facie* showing that it is more likely than not that a utility would not be considered credible. *Id.* That showing must include: (1) a clear statement of the examiner's reasoning; (2) "support for factual finding relied upon in reaching this conclusion"; and (3) support for any PTO conclusions regarding evidence provided by the applicant; and (4) "specific evidence" supporting "any" fact-based assertions needed for the *prima facie* case. *Id.*

The Examiner has made no attempt to satisfy the requirements of these guidelines. The absence of any "specific evidence" warranting a conclusion that each asserted utility is not credible to a person of ordinary skill in the art should mandate withdrawal of the rejection.

III. THE ENABLEMENT REQUIREMENT FOR THE CLAIMED INVENTIONS HAS BEEN MET.

Claims 1 and 3 were rejected as not being enabled under the first paragraph of 35 U.S.C. § 112 because they are not enabled by the specification (Office Action at 5). This rejection has been overcome by the arguments regarding utility, which are incorporated here in their entirety.

Whether the present application is enabling is a question of law. *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 960 n.6, 220 U.S.P.Q. 592, 599 n.6 (Fed. Cir. 1983). The "how to use" prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. §101 that the specification disclose a matter of fact a practical utility for the invention. *In re Ziegler,* 992 F.2d 1197, 1200, 26 U.S.P.Q.2d 1600, 1603 (Fed. Cir. 1993); *Cross v. Iizuka*, 735 F.2d 1040, 1042-44, 224 U.S.P.Q.2d 739, 741-42 (Fed. Cir. 1985) (section 112 is not satisfied if the application does not disclose a practical utility for the invention within section 101); *In re Fouche*, 439 F.2d 1237, 1243, 169 U.S.P.Q. 429, 434 (C.C.P.A. 1971) (if "compositions are in fact useless, [Applicant's] specification cannot have taught how to use them."). No contention has been made that one of ordinary skill in the art could not use the invention for the recited utilities. Having established the sufficiency of those utilities under 35 U.S.C. §101, withdrawal of the pending rejection of claims 1 and 3 for lack of enablement is requested.

The foregoing analysis should be dispositive of the enablement rejection articulated by the Patent Office. In the sentence bridging pages 7 and 8 of the Office Action, however, the Patent Office asserts that making and testing the suitability of the nucleic acid molecules embraced by the claims "would require excessive trial and error experimentation due to the unpredictability involved, and would therefore require undue experimentation." This statement appears to be made only in reference to the use of the nucleic acid molecules as a probe or primer. It has no bearing on the other stated utilities in the specification and should therefor be withdrawn as a basis for the rejection. For completeness, however, further analysis of "undue experimentation" is provided below.

In re Wands sets forth eight criteria to be considered in determining whether a claimed invention would require undue experimentation. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Reasonable analysis of these criteria also leads to the conclusion that the claimed invention would not require undue experimentation.

The first criteria that should be considered is the quantity of experimentation necessary, although a considerable amount of experimentation is permissible if it is routine. *Id.* While the

claimed invention encompasses a broad class of nucleic acid molecules, it would be well within the routine skills of a person of ordinary skill in the art to make and use many members of that class. For example, the addition of either nucleotides to a disclosed sequence is well within the skill of those working in this technology. (Specification at page 16, lines 4-10, page 25, lines 1-19, page 46, lines 4-11, page 46 line 20 through page 54, line 14, page 66, line 26 through page 67, line 6). In addition, standard resource materials that describe specific conditions and procedures for the construction, manipulation and isolation of macromolecules is referred to at page 66, line 26 through page 67, line 6 of the Specification.

The second criteria is the amount of direction or guidance presented. The Specification provides both specific and general guidance to those of ordinary skill in the art. One example of the specific guidance disclosed is that the nucleic acid may be labeled with, for example, fluorescent, chemical or modified bases. (Specification at page 16, lines 4 through 8). An example of the general guidance provided to those of ordinary skill in the art include the direction within the Specification to standard resource materials which describe specific conditions and procedures for the construction, manipulation and isolation of macromolecules. (Specification at page 66, line 26 through page 67 line 6).

The third criteria is the presence or absence of working examples. Examples 1 and 2 are such working examples. They disclose the preparation of a cDNA library in a bacterial vector (plasmids). Example 2 discloses that the plasmids may be partially sequenced to generate ESTs and that such plasmids can and do contain additional nucleotides to those sequenced such as those present within the vector (pSport).

The fourth criteria focuses on the nature of the invention, here nucleic acid molecules comprising, consisting essentially of or containing SEQ ID No. 1 or its complement. The nucleic acid sequence of SEQ ID No. 1 is disclosed. Moreover, the nature of the claimed invention involves modifying nucleic acid molecules. Practitioners in this art are prepared to utilize multiple known methods to obtain the desired result. Other such methods will include screening to obtain the desired result.

The fifth criteria focuses on the state of the prior art. Methods needed to practice the invention are known in the art. *See*, for example, Sambook *et al., Molecular Cloning: A Laboratory Manual,* Cold Spring Harbor (1989), Mailga *et al., Methods in Plant Molecular Biology,* Cold Spring Harbor (1995) and Birren *et al., Genome Analysis: Analyzing DNA,* 1, Cold Spring Harbor (1997).

The sixth criteria to be considered is the relative skill in the art. A determination of the relative skill in art to construct, manipulate and isolation macromolecules particularly nucleic acid molecules can be guided, at least in part, by reference to standard resources such as Sambook *et al., Molecular Cloning: A Laboratory Manual,* Cold Spring Harbor (1989), Mailga *et al., Methods in Plant Molecular Biology,* Cold Spring Harbor (1995) and Birren *et al., Genome Analysis: Analyzing DNA,* 1, Cold Spring Harbor (1997). At a minimum, the relative skill in the art is a person would be able to construct, manipulate and isolation macromolecules in the manner described by such references.

The seventh criteria considers the predictability of the art. The art to consider here, of course, is that art associated with modifying nucleic acid molecules. While the resultant biological properties of a modified nucleic acid molecule may, in certain circumstances, be difficult to predict that is not the appropriate analysis. The analysis to be undertaken is whether known methods to modify nucleic acid molecules are sufficiently predictable. Methods to modify nucleic acid molecules are both routine and well-known (*See,* for example, Sambook *et al., Molecular Cloning: A Laboratory Manual,* Cold Spring Harbor (1989), Mailga *et al., Methods in Plant Molecular Biology,* Cold Spring Harbor (1995) and Birren *et al., Genome Analysis: Analyzing DNA,* 1, Cold Spring Harbor (1997)).

The eighth criteria focuses on the breath of the claims. Here the rejected claims recite traditional open and semi-open transitional terms, "comprising" and "consisting essentially of". The use of such open or semi-open language does not alter the fact that these claims, while broad, are enabled. Not every species encompassed by the claims needs to be disclosed, even in an unpredictable technology. *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 218

(C.C.P.A. 1976). Enablement is satisfied when its disclosure "adequately guide[s] the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility." *See In re Vaeck*, 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991).

Consideration of the *Wands* factors clearly establishes that undue experimentation would not be required to practice the invention. The Specification provides considerable direction and guidance and provides working examples. There was a high level of skill in the pertinent art at time the application was filed and methods to practice the claimed invention were known. Moreover, practitioners of this art are prepared to screen populations of molecules to obtain the desired result. Such screening is routine and does not require undue experimentation.

Even for utility as a probe or primer, however, nothing more than routine experimentation would be required to determine how to make and use the claimed nucleic acid molecules. (Specification at, for example, page 16, line 1 through page 19 line 3, page 24 line 13 through page 27 line 8, page 66, line 25 through page 67, line 6). Performing routine and well-known steps cannot create undue experimentation even if it is laborious. *See In re Wands*, 858 F.2d at 737, 8 U.S.P.Q.2d at 1404; *In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-19 (C.C.P.A. 1976). This rejection, if it is a separate basis for rejection, should therefore also be withdrawn.

The sentence bridging pages 7 and 8 might also be interpreted as a statement that inoperative embodiments may be included in the claimed nucleic acid molecules (Office Action at 7-8). That contention would be irrelevant. "It is not a function of the claims to specifically exclude . . . possible inoperative substances." *Atlas Powder Co. v. E. I. Du Pont de Nemours & Co.*, 750 F.2d 1569, 1576, 224 U.S.P.Q. 409, 414 (Fed. Cir. 1984) (citing *In re Dinh-Nguyen,* 492 F.2d 856, 858-59, 181 U.S.P.Q. 46, 48 (C.C.P.A. 1974). Moreover, the Patent Office has not met its burden in showing that there are an excessive number of inoperative embodiments, even for this limited use. Without such a showing, there is no reason to question the enablement of the claims.

IV. THE CLAIMS SATISFY THE WRITTEN DESCRIPTION REQUIREMENT

The Patent Office rejected claims 1-4 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. (Office Action at 8). The rejection is apparently for undue breadth. "The disclosure of the single nucleic acid molecule . . . does not adequately describe the infinity of . . . molecules embraced by claims 1, 3 and 4." (Office Action at 8-9). "Overbreadth" was long ago "discredited as a basis for determining the sufficiency of a specification." *United States Steel v. Phillips Petroleum Company*, 865 F.2d 1247, 1251, 9 U.S.P.Q.2d 1461, 1464 (Fed. Cir. 1989) (citing *In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971). For that reason alone this rejection should be withdrawn.

Whether the written description requirement has been met is a question of fact. *Vas Cath v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); *Regents of the U. of Cal. v. Eli Lilly*, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404 (Fed. Cir. 1997). If a person of ordinary skill in the art would have understood the inventor to have had possession of the claimed invention, even if not every nuance, then the written description requirement is met. *In re Alton*, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d 1578, 1584 (Fed. Cir. 1996). An applicant is not required to "describe", in the sense of 35 U.S.C. § 112, all things that are encompassed by the claims. To contend otherwise would ignore established jurisprudence in which technology developed after a patent issues has been held to infringe that patent. *United States Steel v. Phillips,* 865 F.2d at 1251, 9 U.S.P.Q.2d at 1464. Thus, even though the present claim would be asserted to encompass a gene sequence that includes the recited EST sequence, there is no requirement to "describe" that gene sequence or other variations that may be created by adding additional nucleotides on either end of the sequence.

An adequate written description of a DNA coding for a particular protein requires a precise definition, for example, by structure, formula, chemical name *etc.*, not a mere wish or

plan for obtaining the claimed molecule. *Regents of the U. of Cal. v. Eli Lilly & Co.*, 119 F.3d at 1566, 43 U.S.P.Q.2d at 1404; *Fiers v. Revel*, 984 F.2d 1164, 1170, 25 U.S.P.Q.2d 1601, 1606 (Fed. Cir. 1993). That has been done here by reciting the nucleotide sequence of 469 nucleotides.

In *Regents v. Eli Lilly*, 119 F.3d at 1562-63, 43 U.S.P.Q.2d at 1401, the claims at issue did not recite a nucleotide sequence. They were instead drawn to any nucleotide sequence coding for insulin or human pro-insulin, a specific protein. The specification described only the nucleic acid sequence coding for rat insulin. *Regents v. Eli Lilly*, 119 F.3d at 1568, 43 U.S.P.Q.2d at 1405. Here, unlike *Lilly*, applicants describe and claim a specific sequence of nucleotides. Thus, applicants have undoubtedly "described" the recited sequence and possession of the claimed invention. Although the claims at issue may be asserted to cover sequences that include the recited sequences joined with additional sequences, this does not raise a written description issue.

The same distinction applies to *Fiers*. There the claim[5] at issue was "a DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide." The present claims recite a specific nucleotide sequence, not a genus of unspecified genes.

Conventional principles establish that the claims at issue here are not "unduly broad" or "indefinite". *See In re Borkowski*, 422 F.2d 904, 909-910, 164 U.S.P.Q. 642, 646 (C.C.P.A. 1970). There, claims were rejected as being unduly broad because of the term "hydrocarbon" was used. The claims recited reaction of "hydrocarbons in vapor phase" with ferric chloride in a sequence of steps. The claims were rejected because the word hydrocarbon encompassed a limitless number of substances which had not been exemplified or described. The CCPA explained in the following way that such a rejection would be improper under the first paragraph of 35 U.S.C. § 112:

> [T]here is no magical relation between the number of representative examples and the breadth of the claims; the number

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5 A count was actually involved in *Fiers*.

> and variety of examples are irrelevant if the disclosure is "enabling" and sets forth the "best mode contemplated."

See In re Borkowski, 422 F.2d at 910, 164 U.S.P.Q. at 646. Any sequence containing the nucleic acids of SEQ ID No. 1 will be readily recognized. That is fully supported by the current disclosure. (Specification at, for example, page 16, lines 1 through 10 (describing sequences with labels to facilitate detection), page 21, lines 1 through 9 (describing fusion nucleic acid molecules), page 25, lines 1 through 19 (describing automated nucleic acid synthesizers to build nucleic acid molecules), and page 66, line 25 through page 67, line 6 (citing references describing the construction manipulation and isolation of nucleic acid macromolecules)). In particular, the references cited in the specification on page 67, line 2 through line 6, exemplify that a person skilled in the art would envision adequate written description support for the claimed molecules -- *i.e.* nucleic acid molecules either comprising or consisting essentially of SEQ ID No. 1. The fact that nucleic acid sequences may be added to either end of the recited sequence is beside the point. Applicants have therefore reasonably conveyed to one skilled in the art possession of the claimed invention, even when additional sequences are added to either end. That should end the analysis.

The use of open claiming language (comprising) or semi-open claiming (consisting essentially of) does not alter the fact that a skilled artisan would readily envision adequate written description support. Indeed, as illustrated by the references cited at page 67, line 2 through line 6, the additional of, for example, detectable labels or extra nucleotides are readily envisioned by those of ordinary skill upon reading the present specification.

As one skilled in the art clearly could envision the claimed molecules, claims 1 and 3 clearly satisfy § 112, first paragraph.

V. THE CLAIMS ARE NOT INDEFINITE

The Patent Office rejected claims 1-4 under 35 U.S.C. § 112, second paragraph, as being "indefinite" for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. (Office Action at 9).[6]

Compliance with the definiteness requirement of § 112, second paragraph, is a question of law that asks no more than if the claims, read in light of the specification, reasonably apprise those skilled in the art of the scope of the invention. *See Credle v. Bond,* 25 F.3d 1566, 1576, 30 U.S.P.Q.2d 1911, 1919 (Fed. Cir. 1994). The focus of the question revolves around a reasonable understanding of one of ordinary skill in the art. *In re Miller,* 441 F.2d 689, 692-93, 169 U.S.P.Q. 597, 599 (C.C.P.A. 1971). Furthermore, the scope of the invention defined by the claims is a matter for § 112, first paragraph, not § 112, second paragraph. *In re Borkowski*, 422 F.2d at 904, 164 U.S.P.Q. at 646. Here, as discussed in the prior section, the claims clearly recite structure by reference to a specific sequence of nucleic acids. Because a person of skill in this technology could discern whether a new sequence contained SEQ ID No. 1 or its complement, the claims are definite. The fact that the entire chemical structure of compositions encompassed by the claims is not positively identified is immaterial. *See id.* Having described the specific structure of nucleic acids, there is no need to add words of limitation to satisfy the "definiteness" requirement. While the absence of additional structural limitations obviously broadens the claim, it does not render the claims indefinite. Indeed, "the absence of the limitation has a precise meaning." *In re Fischer*, 427 F.2d 833, 838, 166 U.S.P.Q. 18, 23 (C.C.P.A. 1970) (reversing an indefiniteness rejection of a claim with an explanation that although the absence of a limitation to amino acids beyond the 24th position obviously broadens the claim and raised questions of sufficiency of disclosure, it does not render the claim indefinite).[7] Regardless of the

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[6] To expedite prosecution, claim 4 has been canceled. The rejection as applied to claim 4 is therefore now moot. Also to expedite prosecution, the word "isolated" has been substituted for the phrase "substantially purified", without prejudice. The rejection under § 112, second paragraph, as it applies to the deleted language is now moot.

[7] The sufficiency of the written description is discussed in section IV.

specification, the claimed subject matter is in no way limited by the presence or absence of sequences added to either end of the recited structure. *Id.* That should end the analysis of indefiniteness.

The Patent Office contends that the recitation "consisting essentially of" renders claim 3 vague and indefinite "since it is unclear how 'consisting essentially of' alters the scope of claim 3 [when] compared to claim 1, which recites 'comprising.'" (Office Action at 5, 10, and 11). These statements appear to question the definiteness of claim 1.

Both claims 1, 2 and 3 recite SEQ ID No. 1 in the body of the claims. The transitional terms, however, differ. The Patent Office asserts that the difference in scope conveyed by these different transitional terms, cannot be understood sufficiently for one to determine the metes and bounds of at least claim 3. The Examiner reasons that since the "specification does not explicitly disclose any nucleic acid molecules that "comprise" SEQ ID No. 1 or a fragment thereof, other than SEQ ID No. 1 itself and fragments of it" (Office Action at 6), and "because the specification does not clearly and explicitly define the basic and novel characteristic of the core nucleic acid sequence set forth as SEQ ID No. 1" (Office Action at 10), one could not determine whether or not a nucleic acid as claimed in claim 3 retains the basic and novel characteristic of SEQ ID No. 1. Regardless of the specification, the claimed subject matter is in no way limited by the presence, absence of sequence added to either end of the recited sequence. *Id.*

Applicants chose to use common transitional terms in their claims. There is nothing vague about these terms and how the law defines them. In fact, as stated many times before, the transitional terms "comprising" and "consisting essentially of" are terms of the patent drafter's art. *See Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1574, 224 U.S.P.Q. 409, 412 (Fed. Cir. 1984) (defining "consisting essentially of" as a phrase that excludes ingredients that may materially affect the basic and novel characteristics of the claimed composition); *Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 1271, 229 U.S.P.Q. 805, 812 (Fed. Cir. 1986) (defining "comprising" as a term that means that the claim does not exclude additional unrecited elements). One skilled in the art would not require a Federal Court's

decision on claim construction to be reasonably apprised of the claim scope simply because a claim uses these legal, transitional terms. That would not be a "reasonable" way to define any claim. When a specification does not alter their meaning, the use of a transitional term in connection with defining the varying scope of an invention cannot be the basis for any indefiniteness, regardless of the specification's content. Applicants do not in any way alter the common meaning of these terms.

Summarizing the above, one skilled in the art is reasonably apprised of the sequence of the claimed nucleic acid molecules from the recited SEQ ID No. 1. One is also reasonably apprised of what differences from a nucleic acid of SEQ ID No. 1 the claims encompass from the use of permissible transitional terms. The Examiner points to no other reason for this rejection. The Patent Office, therefore, has failed to show that applicants' claims do not satisfy § 112, second paragraph.

In justifying this rejection, the Patent Office relies on arguments that a nucleic acid "comprising" SEQ ID No. 1 is not defined in the specification and that the basic and novel characteristics of SEQ ID No. 1 cannot be determined. As noted above, "comprising" is a term well know in patent drafting. Applicants do not assert any definition that differs from that which the case law provides. Furthermore, the basic and novel characteristic of a nucleic acid molecule includes its nucleic acid sequence. Thus, the sequence found in SEQ ID No. 1 defines at least one possible basic and novel characteristic. Accordingly, one skilled in the art could reasonably determine the scope of both of claims 1 and 3.

The assertion that a nucleic acid molecule "comprising SEQ ID No. 1" creates confusion in one's ability to reasonably be apprised of the invention has no merit. One skilled in the art clearly knows if a molecule comprises SEQ ID No. 1 or its complement. One skilled in the art also knows what materially effects the basic and novel characteristics of a nucleic acid sequence or its complement. Thus, both of claims 1 and 3 satisfy § 112, second paragraph.

VI. THE REJECTIONS UNDER 35 U.S.C. §102(b) FOR ANTICIPATION HAVE BEEN OVERCOME BY SUBSTITUTION OF "ISOLATED" FOR THE PHRASE "SUBSTANTIALLY PURIFIED."

Claims 1, 3 and 4 were rejected under 35 U.S.C. §102(b) as being anticipated by Reams. The premise of that rejection was that phrase "substantially purified" as defined in the specification, caused the claim to read on the cited art. That phrase has now been replaced by the term "isolated" as explained in the Remarks section of this Response. That substitution obviates the anticipated rejection and warrants withdrawal of the rejection.

Claims 1, 2 and 4 were also rejected under 35 U.S.C. §102(b) as being anticipated by *Choi et al.* That rejection was also premised on the scope of the phase "substantially purified." The same reasons for withdrawing the rejection in view of Reams warrant withdrawal of the rejection in view of *Choi.*

The separate rejection of claim 4 under 35 U.S.C. §102 in view *Shen et al.* has been rendered moot by cancellation of claim 4 without prejudice.

Respectfully submitted,

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